CLINICAL PROCEEDINGS

of the

CHILDREN'S HOSPITAL

WASHINGTON, D. C.

March 1953

VOLUME IX NUMBER 3

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OF THE CHILDRENS HOSPITAL

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CERVICAL MASSES IN CHILDREN

Special Report No. 257

Marshall C. Sanford, M.D.

Physicians frequently are called upon to evaluate cervical masses in children. This discussion will include the more important conditions to be considered when examining a child with a mass in the neck. No attempt will be made to list all of the conditions which can produce cervical masses since a complete differential diagnosis can be found in any current text on the subject.

In the neck some of the most vital structures of the body are found. The embryological origins of these structures are varied. Ward and Hendricks[1] have said:

> Because of the numerous and varied structures confined within a small space, a tumor, benign or malignant, arising in any one organ soon presses upon or invades those adjacent, making the problem of diagnosis and therapy complex and complicated.

Cervical masses are common in childhood and the importance of early diagnosis and careful evaluation cannot be too strongly emphasized. Early detection is possible in most cases since the area is so accessible.

The diagnosis is established by the employment of routine techniques, the most important of which should include a careful history and physical examination. Many enlargements involve the lymph nodes, and, obviously, the differentiation between localized and generalized lymphadenopathy is essential. Those children who have generalized lymphadenopathy which may be associated with systemic disease will not be included in this discussion; rather, the emphasis will be placed upon the identification of a solitary cervical mass discovered either during a routine physical examination or encountered as the presenting complaint.

The physical examination includes careful investigation of the entire body as well as the local tumor. One must determine the physical characteristics and the exact position of the mass. Valuable information is obtained from its relationship to adjacent structures; whether or not it is discrete, tender, fluctuant, or moveable and whether or not it is altered by swallowing, straining or by inspiration or expiration. X-rays and blood studies may aid in the exclusion of tuberculosis or syphilis. Needle aspiration or biopsy of cystic or fluctuant areas may be indicated although surgical exploration and biopsy usually are the most satisfactory methods of establishing a definite diagnosis.

Cole and Elman[2] have divided cervical tumorfactions into neoplastic, cystic, inflammatory, and miscellaneous groups, while others have con-

sidered them as originating in the lymph nodes or in other structures. This latter classification seems more suitable for our discussion.

CERVICAL MASSES OF LYMPH NODE ORIGIN

The cervical lymph nodes are divided into three main groups. The largest group is the posterior cervical chain. It is located on both sides of the neck along the posterior margin of the sternocleido-mastoid muscle. Those in the anteriolateral portion of the neck constitute the second group and frequently are involved in various inflammatory processes originating in the mouth. The last group are the submental nodes which are located under the chin and in the submandibular area, and are the least common sites of tumorfaction.

Pyogenic Infections: Acute or chronic lymphadenitis is regional and always secondary to inflammation elsewhere. Careful examination of the area drained by these nodes may disclose the causative factor. The mass is hot, tender, usually discrete, and may be associated with anorexia, malaise, and prostration. The infection rarely progresses to actual suppuration, but may do so if the infection is massive or if the nodes are quite superficial. Treatment is directed towards eliminating the etiological agent, e.g., extraction of an abscessed tooth or drainage of a localized scalp infection. In most cases, the administration of antibiotics, local heat and supportive therapy is sufficient.

Tuberculous Infections: Lymphadenitis or actual "cold abscess" may be differentiated from the pyogenic infections since the process is more slowly-progressive, and is often a smouldering one. The nodes may become enlarged, fused or matted together, may be almost non-tender and exhibit very little local reaction. If these nodes are allowed to break down and drain externally, they show a definite tendency toward chronicity. Treatment is directed towards avoiding suppuration. Incision and drainage should be avoided whenever possible in patients in whom this diagnosis is suspected. Aspiration of a fluctuant node may establish the diagnosis, but the fluctuant area should be approached by inserting a long needle through normal tissues rather than by puncturing directly into the abscess. Non-suppurative tuberculous lymphadenitis may require actual excision of the involved nodes. Although this procedure is not performed so frequently as in the past, it can be carried out safely with the use of streptomycin as an adjunct.

Lymphomas: In this group we include those cases of Hodgkin's disease, lymphosarcoma, and leukemia in which a discrete cervical mass is the first manifestation of the condition. The nodes are discrete, firm, non-tender, and non-suppurative. Roentgenographic studies may visualize enlargement of the mediastinal nodes due to a lymphoma, or blood studies may

establish the diagnosis of leukemia. Surgical biopsy of the lymph node and bone marrow examination are the usual procedures in establishing the diagnosis. The disease itself determines the specific therapy to be employed.

Metastases from a carcinoma or sarcoma may present as an isolated cervical mass. They are usually very firm, non-tender, non-inflammatory and discrete. Sometimes the appearance of the mass is the first indication that a neoplastic tumor is present. Careful search often reveals the primary source. Biopsy is the only satisfactory method of establishing the diagnosis, and therapy depends on the site and type of the primary tumor and the extent of lymph node involvement.

Cat Scratch Disease: This entity, although recognized for many years, has received relatively little attention until quite recently when Daniels and MacMurray[4, 5] reemphasized its importance. A history of contact with cats, regional lymphadenopathy, a positive intradermal reaction to the injected antigen, and specific histological changes in biopsied lymph nodes confirm the diagnosis. The lymph nodes become riddled with abscesses which tend to adhere to adjacent structures, and long-burrowing tracts are found in the matted tissue. The frequency of children's contact with cats makes this entity an important one. Fortunately, the condition is not a serious one and is self-limited. Biopsy is indicated to establish the diagnosis and to rule out some of the more serious entities with which it may be confused.[3]

CERVICAL MASSES NOT OF LYMPH NODE ORIGIN

Benign Tumors of the Skin and Subcutaneous Tissue: These include moles, warts, lipomas, fibromas, nevi, cartilagenous nodules under the skin, and sebaceous cysts. These masses usually are small, soft, or rubbery; move freely; and are unattached to the deeper structures. Their character is not difficult to determine on physical examination alone. Treatment consists of simple excision.

Cystic Hygroma or Lymphangioma could be included with the discussion of other benign tumors of the skin and subcutaneous tissues, but because their management is so different, they will be discussed separately. Cystic hygromas are found in many areas but are most common in the neck and often extend over the shoulder or back. Most often they are soft, cystic, multilocular structures with indistinct margins. When there is a mediastinal component present, these tumors will change position with respiration. They disappear on inspiration and are forced out of the mediastinum on expiration. Although benign pathologically, their invasive tendency makes them malignant in character. Recurrences are common following excision, unless all portions of the mass are completely removed. The treatment of

choice consists of early and complete removal of all of the lymphangiomatous tissue. Sometimes, when this is not possible, the use of sclerosing agents may be of merit.

Branchial Cleft Cysts are usually located in the lateral portions of the neck. A sinus from the cyst to the skin is often present, but may be so small that it escapes detection. Only the mass itself will be present unless the sinus is patent. Drainage, when present, is usually intermittent and may be associated with varying degrees of infection in the cysts. The mass may vary in size from 2 to 6 centimeters in diameter; it does not move with swallowing, and is not tender unless infected. Treatment consists of complete excision of the cyst together with the sinus, if one is present.

Thyroglossal Duct Cysts present as midline masses. They move with swallowing and often possess an accompanying sinus. A small tract leading from the skin sinus upward in the direction of the floor of the mouth may be identified. This tract goes through the hyoid bone and terminates at the base of the tongue. These cysts often become infected, and intermittent drainage from a small midline skin sinus may be the presenting complaint. Excision of the mass together with the entire tract and part of the hyoid bone is the only treatment which will prevent a recurrence.

Dermoid Cysts may be located in the midline or in the lateral cervical regions. Usually, they are non-tender, well circumscribed and show little tendency toward sinus formation. They are uncommon and often may be confused with branchial cleft cysts. Dermoid cysts do not have a characteristic x-ray appearance as do many of the teratomas to which they are closely related. The discreteness of both of these masses facilitates excision which is the method of management.

Thyroid: The diagnosis of masses arising in or associated with the thyroid gland is not difficult. Their location and movement during swallowing are clues to their identity. Adenoma, diffuse hyperplasia, cyst or carcinoma may appear as a solitary tumor in or near the midline. More than one-fourth of all thyroid masses in children are neoplastic. Confusion often results when the appearance of lateral metastasis in the regional lymph nodes is the first suggestion of a carcinoma in one lobe of the thyroid gland. Minute primary tumors may give rise to large metastatic nodules. Misplaced thyroid tissue located laterally or at the base of the tongue occasionally can cause confusion. Exploration and resection are indicated in all except diffuse hyperplasia of the gland.

Vascular: Aneurysms or Arterio-Venous Fistulas are very rare, and usually are traumatic in origin. A thrill, murmur and pulsation of the mass reveal its identity. *Hematoma* is usually traumatic but may result from a blood dyscrasia. In a newborn, a hematoma in the belly of the sternocleido-

mastoid muscle is unmistakable and, if appropriate steps are taken, torticollis may be prevented. *Phlebectasia* of the jugular vein produces a soft, rounded mass which increases in size with straining and casts an opaque shadow on x-ray examination. Ligation or excision of the involved vessel corrects the condition.

Esophageal Diverticulum or Pharyngeal Pouch are not common in children. They may cause a localized cervical mass, but symptoms such as regurgitation, dysphagia or "noise in the throat" attract attention first. Most of these lesions present themselves on the left side of the neck just anterior to the sternocleido-mastoid muscle. Complete excision, in one stage, is now the accepted method of treatment.

SUMMARY

1. Cervical masses are common in children.
2. Some of the more important conditions producing isolated cervical masses are outlined.
3. The importance of early diagnosis and treatment is emphasized.

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HYPOVENTILATION SYNDROME

Case Report No. 258

Joseph M. LoPresti, M.D.
John A. Doyle, M.D.

INTRODUCTION

The following case is reported to illustrate a recently described form of respiratory irregularity which may occur in patients with bulbar poliomyelitis.

CASE REPORT

W. H., a three-year old white male was admitted to Children's Hospital on August 22, 1952 with the chief complaints of abdominal pain, fever, and vomiting of one day's duration. The physical examination revealed an acutely ill white male whose temperature was 101.0 F.; pulse, 130, and respirations, 30 per minute. Nuchal and back rigidity were present; the deep reflexes were hypoactive, and bilateral hamstring spasm was noted. Two days after hospitalization, the temperature was 102.0 F.; pulse, 160, and respirations, 40 per minute. Physical examination revealed right facial weakness, paralysis of all four extremities, and weakness of the intercostal muscles. Admission spinal fluid findings revealed 291 white blood cells with 84 per cent polymorphonuclear cells and 16 per cent lymphocytes. Spinal fluid protein was 57 milligrams per 100 milliliters.

The patient was placed in a tank respirator. He became afebrile on the fifth hospital day, and on the sixth day was able to remain out of the respirator. On this day the patient was noted to be lethargic and his respirations, Cheyne-Stokes in type. The respiratory rate was 44 per minute. He was returned to the respirator, but no improvement was noted. He was then placed in an oxygen tent. Within a few minutes the respiratory rate fell to 30 per minute; the respiratory excursion became more shallow, and the lethargy increased to a point where external stimulation did not arouse him. On discontinuance of the oxygen, the respiratory rate again increased to 44 per minute and the respiratory excursion became less shallow; however, the lethargy persisted although the patient responded to external stimulation. A diagnosis of the hypoventilation syndrome was made and the electrophrenic respirator was instituted for 20 minutes. Shortly after diaphragmatic excursions were established, the patient opened his eyes, became alert, and responded to questioning. Eight hours later, he again lapsed into his original lethargic state and the electrophrenic respirator was used for 30 minutes. A similar dramatic and beneficial effect was obtained. Since that time the patient's sensorium remained clear.

DISCUSSION

It has long been recognized in patients with poliomyelitis that respiratory embarrassment and/or irregularities fall into two large categories:

1. High spinal thoracic involvement with paralysis or weakness of the muscles of respiration. In this type of involvement, the patient retains his central control of respiration and, therefore, the respirations, though rapid, are usually regular.

2. Involvement of the respiratory center in patients with bulbar poliomyelitis. In this group, the patient partially has lost central control of respirations. The respiratory rhythm, therefore, is grossly irregular and clinically may be easily differentiated from the first group.

In 1917, Sarnoff, et al.[1] reported a third type of respiratory irregularity which may occur occasionally in bulbar poliomyelitis. These investigators termed such involvement the hypoventilation syndrome. This syndrome is not a new disease entity in clinical medicine. It is caused by a decreased sensitivity of the respiratory center to the carbon dioxide content of the plasma. Marshall and Rosenfeld[2] produced the hypoventilation syndrome in experimental animals anesthetized with barbiturates and morphine.

A similar loss of respiratory center sensitivity to carbon dioxide in patients with advanced emphysema was demonstrated in 1920 by Scott.[3]

The clinical features of this syndrome are apparent on close observation of the patient. Drowsiness, lethargy, and disorientation are present invariably. The skin becomes pale, ashen, and at times slightly cyanotic. The outstanding manifestations are noted in the respiratory system. The respirations become quite shallow for variable periods of time without becoming either rapid or irregular. These periods of hypoventilation alternate irregularly with periods of apparent adequate ventilation. The regular periodicity noted in patients with Cheyne-Stokes respirations is not present. In some patients the duration of the hypoventilation period will last as long as the patient is quiescent and undisturbed. These patients possess full control of their respiratory muscles. *If oxygen is administered the condition becomes worse.*

It remained for Marshall and Rosenfeld[2] to explain the apparent paradox of the accentuation of respiratory depression by the administration of oxygen to patients with the hypoventilation syndrome. An understanding of the altered physico-chemical state as well as the clinical recognition of the syndrome is essential for a rational approach to therapy. In chronic emphysema, the carbon dioxide tension of the blood is elevated persistently and the respiratory center, surrounded by this constant high carbon dioxide medium, becomes insensitive to stimulation by changes in the plasma carbon dioxide tension. This situation is analogous to inhabitants of high altitudes. In barbiturate or morphine intoxication as well as in some central nervous system infections, e.g., encephalitis or bulbar poliomyelitis, the loss of sensitivity to carbon dioxide stimulation is caused by a poisoning of the respiratory center by the toxic agent. In a normal individual with an intact respiratory center, the primary drive to respiratory stimulation is supplied by an increase in the carbon dioxide tension of the blood. Under certain circumstances, e.g., chronic emphysema, barbiturate and morphine intoxication, encephalitis, or poliomyelitis, when the respiratory center becomes insensitive to carbon dioxide stimulation, *respiration is maintained by the accompanying lowered oxygen tension.* This stimulation is mediated via the aortic and carotid sinus bodies. If oxygen is administered to such patients, the oxygen tension of the blood will be raised. As this happens, the stimulus which maintained the respirations in these patients, i.e., the lowered oxygen tension, will have been removed. Hypoventilation in the patient then will increase. The outcome will be a further accumulation of carbon dioxide in the body. Since excessive levels of carbon dioxide not only fail to stimulate breathing but actually depress it[4, 5, 6], the disease may terminate fatally because of the depressing and narcotic effects of carbon dioxide.

This concept assumes paramount importance because the routine ad-

ministration of oxygen to patients with bulbar poliomyelitis is an accepted therapeutic practice. Patients with the hypoventilation syndrome will not be benefited by the administration of oxygen. Indeed, the use of oxygen under such circumstances usually will be detrimental and contraindicated. Having once recognized the altered physiologic state in these patients, the problem becomes one of elimination of carbon dioxide by increased lung ventilation. Evidence has accumulated[7, 8] that the decreased sensitivity of the respiratory center to carbon dioxide in patients with the hypoventilation syndrome is a transient state. If the carbon dioxide tension can be returned to normal, it often will be accompanied by a restored sensitivity of the center to carbon dioxide. In most patients the restoration of this sensitivity may be of lasting benefit. The problem, then, is one of improving ventilatory exchange. This may be accomplished in a number of ways. In some instances, the only measure necessary will be supplied by a nurse or attendant who reminds the patient to breathe deeply. However, in most cases the lethargy and drowsiness is so severe that such a measure is not practical. In these patients an artificial aid to ventilation will be necessary. The tank respirator may be considered. If utilized, both negative and positive pressure should be applied. However, since most of these patients have lower cranial nerve involvement, and, therefore, accumulate large amounts of oropharyngeal secretions, the tank respirator may be hazardous. In addition, its use involves a bulky and expensive apparatus which often has an adverse psychological effect on the patient. In recent years, electrophrenic respiration developed by Sarnoff has proved to be an effective, inexpensive, and feasible method of supplying adequate artificial respiration, and improving ventilation. This apparatus has been utilized elsewhere in the management of respiratory irregularities in acute bulbar poliomyelitis[9]. Its use requires anatomical orientation and practice in locating the motor point of the phrenic nerve[10]. It should be stressed that whenever any form of artificial respiration is administered to a patient, the necessity of maintaining a clear airway is of paramount importance. The electrophrenic respirator may be used effectively in patients with the hypoventilation syndrome. Periodic electrophrenic respiration will eliminate carbon dioxide by increasing ventilatory exchange and thus will restore the sensitivity of the respiratory center.

SUMMARY

1. A case of the hypoventilation syndrome occurring during the course of acute bulbar poliomyelitis has been presented.

2. The hypoventilation syndrome with its etiology, clinical symptomatology, pathologic physiology and treatment has been discussed.

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NEUROBLASTOMA MANIFESTED BY AN ENLARGED LIVER IN THE NEWBORN

*Case Report No. 259**

Robert K. Wineland, M.D.

INTRODUCTION

Neuroblastoma, a rapidly growing malignant tumor of the sympathetic nervous system, is one of the most common tumors of infancy and childhood. This neoplasm may arise in any organ containing sympathetic nerve elements such as the adrenal medulla, the sympathetic chain, organs of Zuckerkandl or various retroperitoneal and retropleural ganglia. It may also arise within the brain or cord[3].

Grossly, the tumor is reddish-gray and highly vascular. Early it outgrows its capsule and extends to other tissues. Microscopically the tumor is composed of small cells with dark nuclei resembling lymphocytes. There is often an attempt at pseudorosette formation.

The signs and symptoms of neuroblastoma are quite variable, and depend on the location, the degree of malignancy, and whether or not metastases have occurred. The first sign is often a firm mass in the abdomen. Enlargement of the liver secondary to metastases is frequently a presenting sign. Symptoms may consist of pain, anorexia, fever, weight loss, constipation or diarrhea[5]. Metastases usually account for the pain. They may occur

* N.B.: Admitted to the private service of William F. Burdick, M.D.

early and generally involve the soft tissues, the orbit and meninges, and almost all parts of the skeletal system—most often with bilateral distribution. Pressure changes detected by the intravenous pyelogram are helpful in diagnosis. Difficulty may be encountered in differentiating this tumor from Wilms' tumor, hydronephrosis, mesenteric, cyst, adrenal hemorrhage and other conditions.

Treatment should follow the principles outlined by Farber for neoplasms in children[1] as follows:

1. Every solid tumor in a child should be considered malignant until proved otherwise by microscopic examination of the removed tissue.
2. Removal of the tumor should be effected without delay after a short 24 to 48 hour diagnostic work-up and pre-operative preparation.

Radiation therapy should be instituted post-operatively since the neuroblastomas are radiosensitive. Farber does not believe pre-operative radiation worthwhile due to the length of time required to effect improvement thus delaying surgical removal.

The prognosis was formerly considered hopeless, but Farber reports 10 of 40 patients who were alive 3 to 8 years after discovery of the tumor[1]. The tumor may:

1. Undergo spontaneous maturation to a benign ganglioneuroma.
2. Undergo spontaneous hemorrhage and necrosis and disappear.
3. Be cured by local irradiation even after metastases have occurred.

Complete recovery has been produced by the use of radiation therapy even after histologically proved metastases to the liver from a primary tumor of the adrenal has taken place[3]. No cure ever has been reported after the bones have been involved.

The following summary of the case record of a newborn infant with an enlarged liver due to metastatic neuroblastoma is presented.

CASE REPORT

C. J., Hospital No. 52-13606.

This three-week old white female was admitted to the hospital on November 20, 1952, at which time a mass was discovered occupying a large portion of the right upper quadrant of the abdomen. Other than several episodes of mild regurgitation which responded to dietary change, the infant had been asymptomatic.

The child was born normally at term, birth weight was 7 pounds 1 ounce. No abnormalities were noted.

The mother was a 19 year old primipara who was in good health. She had had a partial thyroidectomy for goiter two years previously and a "benign" tumor of her left breast had been removed at the same time.

Physical examination revealed a fairly well-developed, fairly-nourished white female in no apparent distress. The abdomen was protuberant, and a large, firm, smooth mass was found to occupy most of the right upper quadrant. This mass extended diagonally across the upper abdomen 8 centimeters below the ribs on the right and 3 centimeters below on the left. Bilateral inguinal herniae were present,

and the right sac was thought to contain an ovary. Several small shotty axillary and inguinal nodes were present bilaterally. The remainder of the examination was negative.

Laboratory studies:

Hemoglobin 12.1 grams; red blood cells 4,200,000; and white blood cells 21,300 with 57 segmented cells, 13 band forms, and 30 lymphocytes per 100 cells. Platelets were normal; urinalysis, normal. Flat film of the abdomen revealed the liver to be enlarged. Intravenous pyelogram indicated the kidneys to be functioning well, but the anatomical structure of the left kidney was not clearly visualized, however, the pyelogram was considered to be essentially normal. X-ray examination of the chest was normal.

The patient was discharged on November 21, 1952, to be observed on an outpatient basis.

On December 4, 1952, at the age of 5½ weeks, the child was readmitted. Although the infant had been asymptomatic, the liver had increased in size. Her weight was 8 pounds 1½ ounces. Physical examination at this time revealed a fairly well-developed and nourished white female in no apparent distress. The abdomen was protuberant. The previously-described mass in the right upper quadrant now extended to the iliac crest on the right and diagonally occupied the left upper quadrant Several observers thought this mass to be somewhat nodular. The herniae were noted as before. No other changes in the physical findings were noted.

The patient was seen by the members of the Tumor Board who considered hepatoma, neuroblastoma and lipoid storage disease among the diagnostic possibilities. X-ray studies at the time of the second admission disclosed a normal skeletal survey. A flat film of the abdomen showed a large mass on the right. Intravenous pyelogram revealed "poor visualization of the right kidneys but the diagnosis of Wilms' tumor was not favored." Urinalysis was normal, no bile being present. Hemoglobin 11.1 grams; hematocrit 43 per cent; white blood cells 21,200 with 25 segmented polymorphonuclears, 3 band forms, 1 young form, 60 lymphocytes, and 11 monocytes per 100 cells. There was no coagulation defect and the platelets were normal. Tibial marrow showed erythroid hyperplasia.

Other blood examinations included: total bilirubin 0.28 milligrams per 100 milliliters, indirect 0.20, direct 0.08; thymol turbidity 1.2 units, and cephalin flocculation 1 plus. Prothrombin time was normal. Total protein was 4.9 grams, albumin 3.7 grams, globulin 1.2 grams, urea nitrogen 13 milligrams, and sugar 65 milligrams. Spinal fluid was normal.

On December 19, 1952, the child underwent laparotomy for biopsy of the abdominal mass. The liver proved to be enlarged with many small yellowish nodular areas. Exploration of the abdomen could not be completed due to the patient's condition, and it was not possible to examine the left kidney. The right kidney and adrenal seemed normal as did the ovaries and intestinal tract. Microscopic examination of the biopsed liver tissue disclosed metastatic neuroblastoma.

Post-operatively the child had an annoying abdominal distention for several days, and developed a thrombophlebitis of the left leg just above the site of a venous cut-down. Both conditions responded to therapy.

Post-operatively the child was placed on a-methopterin therapy upon the suggestion by the Tumor Board that the child would probably be unable to tolerate the toxic effects of radiation therapy to so large an area.

At present, 6 weeks post-operatively, the patient weighs 8 pounds 5 ounces, and is

12 weeks of age. Feedings of Olac, vegetables and Pablum are taken satisfactorily but weight gain has been very slow. She is apparently asymptomatic. There has been no evidence of further enlargement of the liver. A-methopterin has not appeared to have caused any toxic effects.

SUMMARY

Neuroblastoma in infancy and childhood is discussed and the report of a three weeks old infant with hepatomegaly due to such a tumor is reported.

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CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: John A. Doyle, M.D.
By Invitation: John E. Cassidy, M.D.

This one year white female was in good health until six days previous to admission when she began vomiting, became dehydrated and feverish. She was admitted to a hospital outside of Washington, where a diagnosis of pneumonia was made and a sulfonamide, aureomycin, and penicillin were given. While in the hospital she developed diarrhea. On her sixth hospital day she suddenly became cyanotic and comatose, the blood sugar being 267 milligrams/100 milliliters at this time, for which she was given 40 units of regular insulin with 5 per cent glucose solution over a three hour period. At this point she was transferred to Children's Hospital.

Birth, developmental and feeding histories were normal. Family history was negative for diabetes and other hereditary disease. The only previous illness of the patient which was associated with vomiting, at six months of age, responded to home treatment.

Physical examination on admission revealed a well-developed, very drowsy, dehydrated white female infant, lying quietly in bed. Her temperature was 100° F., pulse 148 and respirations 48 per minute. Her skin was warm, pale and dry. The lungs revealed dullness and decreased breath sounds at the right base. The heart, abdomen and genitalia were negative. Her pupils were small and reacted to light. Neurological examination was essentially negative.

Initial laboratory reports revealed: Blood sugar 900 milligrams/100 milliliters; thymol turbidity 4.4 units; non-protein nitrogen 60 milligrams per cent; blood urea nitrogen 28.2 milligrams per 100 milliliters; carbon dioxide combining power 31 volumes per cent; hematocrit 25 volumes per cent; serum potassium "normal"

early; and eosinophile count 9 per cubic millimeters. The blood was noted to be very lipemic.

Urinalysis: Sugar, brick red; acetone, negative; appearance, clear; reaction, acid; and albumin, 25.

Hemogram: Hemoglobin 11.6 grams; red blood cells 4,400,000; white blood cells 2,900; segmented cells 8; band forms 6; young forms 5; lymphocytes 73; monocytes 2; basophiles 6; platelets were reduced; red blood cells showed anisocytosis. Spinal fluid: clear; no cells; protein 39 milligrams per 100 milliliters; sugar 45 milligrams per 100 milliliters.

The patient was given Hartmann's solution intravenously continuously and a total of 150 units of regular insulin from midnight until 6 a.m. By noon her blood sugar had dropped from 900 milligrams on admission to 24 milligrams. She was given 500 milliliters of 10 per cent glucose solution and the blood sugar returned to 500 milligrams per 100 milliliters in two hours. During the evening 10 units of regular insulin was given and by the morning of the second day her blood sugar had dropped to 50 milligrams.

On the morning of the third hospital day her blood sugar was 425 milligrams for which 15 units of regular insulin was given and within six hours it dropped to 45 milligrams.

The infant was given NPH insulin starting with 3 units a day and increasing to 14 units over a period of five days. The blood sugar during this time varied from 150 to 390 milligrams. Urines during this period showed excessive sugar, but never acetone or diacetic acid.

During her hospitalization the patient remained semi-comatose and nutrition was maintained by intravenous and gavage feedings. Her color was described as being "bronze". X-ray of the chest suggested a bronchitic condition. The patient was given 1 gram of chloromycetin intramuscularly each day. She was afebrile until her fourth hospital day when she spiked a temperature of 104° F., after which it varied from 100° F. to 103° F. The cardiac consultant thought that there was no cardiac pathology present.

The patient developed respiratory difficulty and expired on the eighth hospital day—two weeks after the apparent initial onset of her condition.

DISCUSSION

John E. Cassidy, M.D.

In summary we have a white female infant, who was in apparent good health for the first year of her life. She developed pneumonia and in association with this a severe metabolic disturbance became evident and death followed in a relatively short period of time.

With the evidence at hand we can be certain that the patient had diabetes mellitus. When the blood sugar was first determined it was 267 milligrams per 100 milliliters. She was then given 40 units of insulin and 5 per cent glucose solution intravenously—following which her blood sugar was 900 milligrams per 100 milliliters, demonstrating a marked intolerance to glucose. Glycosuria was constant.

Clinically the patient was lethargic and drowsy and progressed to a comatose state. This occurred despite vigorous insulin and fluid replacement

therapy. The blood sugar levels varied from very high to very low and did not become stabilized. The clinical picture of acidosis was not borne out by the laboratory findings one would expect. The carbon dioxide combining power was 31 volumes per cent but there was never any acetone or diacetic acid demonstrable in the urine. These substances are usually always demonstrable in the urine of patients with acidosis complicating diabetes; however, instances have been reported when these substances were not found in the urine in the presence of severe dehydration and renal damage.

There are several other laboratory findings which should be mentioned. The initial hemogram revealed a leukopenia with slight relative lymphocytosis and a reduction in the thrombocytes. Dr. Doyle assures us that on repeated examinations these changes approached the normal; so that their significance is questionable. In addition, the serum potassium is reported as normal shortly after admission. This would not rule out potassium deficiency since the serum levels are not usually demonstrably lowered until later in the course of events. Another level forty-eight or seventy-two hours later, after considerable fluid and insulin had been given, might have been much lower. Electrocardiographic studies would also have added information along this line.

We know that regulation of carbohydrate metabolism is a complex affair in which the pancreas, pituitary and adrenal glands play important and interrelated roles. It is possible that some lesion of the pituitary or adrenal cortex might explain this deviation from the usual pattern. The eosinophile count of 9 per cubic millimeters would indicate an adequate adrenal cortical function. There is no evidence on which to incriminate the pituitary gland.

The course of our patient then was not the usual one of the good response to insulin and fluid therapy and satisfactory stabilization of the blood sugar levels in a reasonable period of time. We can postulate that this might have been due to hypopotassemia, to the presence of some focus infection, or to involvement of the adrenal cortex or pituitary gland.

I do not believe that even with an autopsy examination a satisfactory explanation will be found for this course of events. Metabolic disturbances are much more satisfactorily investigated in the living than in the dead.

PATHOLOGIC DISCUSSION

John A. Doyle, M.D.

Dr. Cassidy's closing remarks bear repeating in relationship to the case we are discussing. Gross and microscopic autopsy findings in cases of metabolic disturbances are often unsatisfactory in explaining the basic pathology present.

The only finding at autopsy of this patient was a moderately severe bronchopneumonia—a contributing cause of death, but certainly not the basic underlying pathology in this little girl.

The adrenal glands showed no gross or microscopic changes, nor did the pituitary gland. It was felt that this patient would show gross or microscopic evidences of cerebral damage, but such was not the case after careful examination of sections of the brain.

The anatomical pathologist cannot answer many of the questions that are asked him, particularly in relationship to metabolic diseases. In the absence of more definitive anatomical pathology we must conclude that this case is representative of diabetes in a child that did not respond to adequate insulin and fluid therapy, with the added unusual feature of absence of ketone bodies in the urine. Other clinical laboratory examinations (sodium, potassium, calcium) that were not made during life might have enabled us to give a more satisfactory clinico-pathological correlation.

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